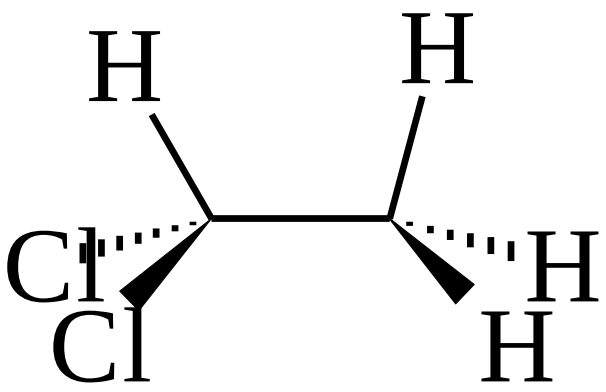
OEHHA

1,1-Dichloroethane (1,1-DCA)



Molecular Weight: 98.96
CAS Registry No.: 75-34-31

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Listing History: 1,1-DCA

- Listed under Proposition 65 on January 1, 1990
- Based on listing (B2) by US EPA, 1989 Health Effects Summary Tables
  - Based on NCI, 1978 bioassay
- US EPA Revised to Group C
  - Lack of evidence in humans
  - Limited evidence in rats and mice

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Carcinogenicity Data Available: 1,1-DCA

- Humans
  - No evidence available
- Animals

  NCI (1978)
  - M/F B6C3F$_1$ mice, gavage, 78 wk (+13 wk obs.)
  - M/F Osborne-Mendel rats, gavage, 78 wk (+33 wk obs.)

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NCI (1978)

Survival (%) at end of study

	Dose group		
	Control	Low	High
Mouse males	55	62	32
Mouse females	80	80	50
Rat males	5	4	8
Rat female	20	16	18

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Tumors in B6C3F$_1$ Mice (NCI, 1978)

1,1-DCA by gavage in corn oil: 78 wk + 13 wk observation		**Dose Group**			
Tumor Site and Type		pooled controls	low	high	Trend
Males					
Liver	Hepatocellular Carcinoma*	6/72	8/48	8/32 (p=0.027)	p=0.016
Females					
Uterus	Endometrial stromal polyps*	0/79	0/47	4/46 (p=0.017)	p=0.005

* Statistically significant association ($p<0.05$) by survival analysis (Gold and Zeiger., 1997)

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Tumors in Osborne-Mendel Rats (NCI, 1978)

1,1-DCA by gavage in corn oil: 78 wk + 33 wk observation		**Dose Group**			
Tumor Site and Type		pooled controls	low	high	
Males					
		No treatment-related tumors			
Females					Trend
Circulatory system	Hemangiosarcoma*	0/39	0/50	4/50 (p=0.09)	p=0.02
Mammary gland	Adenocarcinoma*	1/39	1/50	5/50	p=0.08

* Statistically significant association ($p<0.05$) by survival analysis (Gold and Zeiger, 1997)

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Other Relevant Data

- Tumor promotion studies
  - 1,1-DCA did not exhibit initiating potential
  - 1,1-DCA was positive as a tumor promoter
- DNA binding studies
  - 1,1-DCA administered in vivo to rats and mice resulted in covalent binding to DNA and other macromolecules

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Other Relevant Data

- Genotoxicity

Test System	Response
Reverse Mutation, *S. typhimurium*	-
Reverse Mutation, *S. typhimurium* (closed system)	+
Induction of mitotic segregation, haploids and non-disjuctional haploids; mitotic arrest, *Aspergillus nidulans*	+
Cell transformation assay, BALB/c-3T3	-
DNA-repair test, rat and mouse hepatocytes	+
Viral transformation assay, Syrian Hamster Embryo cells	+
Fluorometric assay of alkaline DNA unwinding, mouse *in vivo*	-

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Structure-Activity Comparisons

- 1,2-DCA: NCI, 1978 (gavage)

	1,2-DCA	1,1-DCA
Male rats		
◆ Forestomach squamous cell carcinomas	✓	
◆ Circulatory system hemangiosarcomas	✓	✓ (females)
Female rats		
◆ Mammary adenocarcinomas	✓	✓
Male mice		
◆ Hepatocellular carcinoma	✓	✓
◆ Lung adenoma	✓	
Female mice		
◆ Endometrial stromal polyps	✓	✓
◆ Lung adenoma	✓	

- 1,2-DCA non-positive by other routes

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Summary: 1,1-DCA

- Carcinogenicity
  - Observations of increased tumor incidences in male mice (liver), female mice (uterus -benign), and female rats (circulatory system and mammary gland)
  - Problems with study quality: high doses, low survival
  - Low tumor incidences
- Other relevant data
  - Positive genotoxicity
  - Chemical structural analogies
  - Tumor promoting activity